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CONTENTS

Editorial:

"A Negligible Trace" 422

Original Articles:

The Evaluation of the Activity of Powders of Veratrum Viride by the
Daphnia Method. By Isadore Cohen 426

Efficiency of Bactericidal Agents in Different Ointment Bases. By
Louis Gershenfeld and Russell E. Brillhart 430

Have a Smoke? By T. Swann Harding 443

Abstracts from, and Reviews of, the Literature of the Sciences Sup-
porting Public Health 450

Solid Extracts 456

Book Reviews 459

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E D I T O R I A L

On these pages the editor offers his opinions, unshackled by advertising patrons and unrestrained by anything save a sense of the decent and the truthful. The editor, alone, is responsible for their type, their tone and their tenor.

"A NEGLIGIBLE TRACE"

THE Pharmacopœia qualifies the above phrase in a quantitative fashion. In "*General Notices*" it states that a negligible trace is ".005 Gm.". Yet we insist that there are imponderable traces much too important to be *neglected*, traces which are yet of such weight and importance that they constitute the tangible intangibles of many of life's most intimate performances. Consider the influence of light on life. Consider the role of the trace of iodine in metabolism. Light and iodine have between them divided the population of earth into the white, the black and the yellow races.

Yes, indeed the most profound reactions, the most intimate reactions in our own bodies are matters of traces.

We know that normal blood contains about five million red corpuscles in each cubic millimeter, but do we realize that the entire blood must therefore contain some twenty-five trillion red cells and thirty billion white cells, figures that have an astronomical aspect? If mental pictures of the billions and trillions of blood cells, crowding and pushing and jostling for a share of the mere teaspoonful of sugar appeal to one's sense of humor, they must also bring home the delicacy of adjustment by which the mechanisms of life are regulated.

Traces, yes—but certainly not "negligible" traces! Elsewhere* someone else has been moved to write of traces and so interesting is the communication that we reprint it here *in toto*.

"The search for gold in sea water, for the needle in a haystack, has always had its appeal. Chemists and metallurgists have long been aware of the effect of the presence of very small quantities of one element on the properties of another. Work such as that of Dr. Brenchley at Rothamsted has made us aware of the need of minimal quantities of certain elements for the satisfactory growth of plants. In the last year or so it has become recognized that animals also, in-

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cluding ourselves, require traces of certain elements for their well-being which hitherto had been thought to have been present in their food only as accidental and inert items.

This discovery, like so many others, has had to wait for the fashioning of the necessary tools or methods with which to detect the traces of the unusual methods. Analytical chemical methods are tedious and costly in time, always the most important factor to the researcher. The modern development of spectroscopy has provided a weapon capable of sufficient accuracy and delicacy and speed of operation; it can be supplemented by the new technique of microchemical analysis originated by Pregel in Vienna, which perhaps more than anything else has made the newest developments in biochemistry possible. Manipulative skill has always played a large part in organic chemical discovery; to-day it is quite remarkable how the small quantities of vitamins and hormones can be isolated from a large bulk of animal material and their analysis and chemical structure determined.

It is perhaps of interest here to follow the story of a few of the more unusual mineral elements, traces of which appear to be essential.

One of these is copper, which has proved to be associated with the formation of hæmoglobin, the red colouring matter of the blood. The condition of anæmia is well known; with rats it can be brought about by simple dietary restriction. The supposed remedy is iron taken in the form of iron salts, but very variable cures were obtained. Indeed, with pure iron salts the rats did not get better, whereas with small doses of liver, known to be a rich source of iron, a rapid cure was effected. Confronted with these facts Professor E. B. Hart set to work, with the zest of the detective in fiction, to track down the curative constituent in the liver. It was soon established that it was something in the ash of the liver and nothing to do with any of its organic constituents. According to the methods of the chemists, the ash was sub-divided into fractions, which were tested separately. It appeared that one alone, containing mercury, arsenic, copper and cadmium compounds, was active, and finally the activity was traced to copper alone, no other metal was of the slightest benefit. When traces of copper are present the rats grow nearly normally; it is better to have some iron present, although iron by itself is useless. The function of the copper is apparently to make the utilization of the iron for hæmoglobin formation possible. In its absence the iron is found

stored up in the liver and spleen; when it is administered new red blood cells are rapidly produced and the stores of iron are used up.

It is not wise to transfer the conclusions derived from experiments with rats directly to man, and it is therefore not certain that he requires copper. Actually, most foods which contain iron are also sources of copper, and the two elements are so hard to separate that even medicinal iron salts contain traces of copper. It is, of course, almost impossible to make experiments of this kind with man; there is at least every probability that we need traces of copper.

Copper deficiency is apparently the cause of 'gingin' disease which involves serious mortality among the lambs in certain districts of Australia. This has been proved to be due to the total lack of copper in the soils of the affected areas. The trouble has been got over by simple dressing of the ground with copper salts or by the provision of copper 'licks.'

Even better known is the malady termed bush disease or costal sickness, which for long was regarded as incurable in Australia and New Zealand, and was responsible for enormous financial losses. Much painstaking research, after a number of false clues had been abandoned, proved conclusively that a shortage of cobalt was the cause of the trouble. Its administration to sick animals is described as having a dramatic effect—an animal that is literally a bag of bones from the effects of the disease is cured in a week. Cobalt salts are easily applied by dressing the pastures.

There is no evidence that the lack of cobalt in the diet has any adverse influence on the rat, whereas the sheep is incapable of living without it. Perhaps the relative size of the two animals and their different food habits may mean that the traces, if any, required by the rat are too small to have been detected. At any rate, there is apparently no need for us to include a 'lick' of the bath tap in our morning toilet.

Work at Rothamsted has shown that pastures in the Dartmoor area are also deficient in cobalt; the sheep there suffer from a disease similar to that in New Zealand.

Another example of the influence of traces is afforded by manganese. This can only be completely withdrawn from the diet of rats at the expense of their reproductive organs, and, indeed, the element is a regular constituent of the reproductive organs both in animals and plants.

The knowledge of these essential elements is still far from complete; the experimental difficulties are very great, particularly in ensuring diets and conditions of living which are entirely free from the element in question. It is already clear that in time other elements will have to be added to the three illustrated—possibly zinc, aluminium, fluorine and even other less abundant elements. The growing knowledge of 'trace elements' in animal nutrition is paralleled with similar progress of their significance for plant growth."

We repeat "Traces—yes! but certainly not *negligible* traces!"

IVOR GRIFFITH.

ORIGINAL ARTICLES

THE EVALUATION OF THE ACTIVITY OF POWDERS OF VERATRUM VIRIDE BY THE DAPHNIA METHOD¹

By Isadore Cohen, Ph. D.²

Philadelphia, Pennsylvania

Introduction

RECENTLY, Viehoveer and Cohen (1) devised a physiological method for the comparative evaluation of the toxicity of preparations of *Veratrum viride* and *V. album* using *Daphnia magna*. The quantitative values obtained by the *Daphnia* method were corroborated by additional assays upon rats, rabbits and guinea pigs.

The action of the extracted veratrum complex upon the locomotion of daphnia is so marked that the degree of impairment to this function (which is also related to the degree of internal depression) can be quantitatively expressed. Fifty standardized daphnia are placed in narrow museum jars (outside measurements 15x10x2 cms.) containing 100 cc. of the test solution made up with culture medium (Bovung) in which the test animals were grown. The swimming of daphnia is a leisurely affair, influenced greatly by the light intensity. Under the influence of the extracted veratrum principles, the swimming activity is accelerated and also incoordinated. During the first phase of veratrum activity, the tendency of the daphnia is to swim upwards. Later, progressive exhaustion forces the daphnia to descend (debility shift) and, finally, the daphnia lie quiescent at the bottom of the observation chamber.

By recording the number of daphnia able to swim above midmark at regularly spaced time intervals, the debility shift is obtained. Under uniform conditions, the rate of the debility shift is directly proportional to the activity of the test solution. When the debility shifts of two or more comparative groups of daphnia fall into the same range, then the activity of the daphnia swimming below the midmark is of especial importance in judging how close the test solutions match.

1. Supported by a grant from Irwin, Neisler & Co., Decatur, Illinois.

2. The author expresses his appreciation of the courtesy of Dr. Leonard G. Rowntree, Director of the Philadelphia Institute for Medical Research, in providing the facilities necessary for the prosecution of this work.

Experimental

I

Two lots of finely powdered *Veratrum viride*, No. 100 and No. 101, were submitted for evaluation. Previous experiments (unpublished) have shown that a potent extract can be prepared by simple aqueous extraction of the powder. Hence, in this preliminary experiment, the following procedure was used. One gram from each lot of powder was extracted by vigorous shaking for 10 minutes in 100 cc. of distilled water and then filtered. The filtrate from No. 100, pH 4.8, contained more green pigment (presumably chlorophyll) than the filtrate from No. 101, pH 5.0. Fifty cubic centimeters of each filtrate were added to fifty unstandardized daphnia in 50 cc. of culture medium contained in the museum jars. The room temperature and that of the test solutions varied from 23 degrees C. to 24 degrees C. during the experiment. Observations were recorded as previously described (1): the number of daphnia swimming above the midmark as the numerator and the number below as the denominator.

Time	No. 100 ($\frac{1}{2}\%$)	No. 101 ($\frac{1}{2}\%$)
1 hour	20/30	10/40
1½ "	30/20	5/45
2 "	25/25	0/50, 2/48, 3/47
3 "	20/30	0/50 (all down, quiescent)

It is apparent from this test that No. 101 is more active than No. 100 in the same concentration. The rapidity of the debility shift may be due to the combination of at least three factors: 1) The daphnia could not be scored as satisfactory for their vitality, 2) The effect of dilution of the culture medium with the distilled water extract, 3) High temperature.

2

One gram from each lot of powder was extracted by vigorous shaking in 100 cc. of culture medium for ten minutes. Again the filtrate from No. 100, pH 5.6, contained more green pigment than the filtrate from No. 101, pH 5.8. The more alkaline pH here is due to the fact that the culture medium is slightly alkaline and possesses an appreciable buffering action. The vitality of the daphnia used in this experiment and the following ones would be scored as satisfactory since wheat germ oil (1 cc./5 gal. culture medium) was used to stimu-

late their reproductive performance. The work reported here was carried out in September. In the preliminary experiment, the daphnia used were from a summering-over culture, low in reproductive performance. The influence of wheat germ oil upon growth and reproduction in *D. magna* has been reported by Viehoveer and Cohen (2).

Fifty cubic centimeters of each filtrate were added to fifty standardized ten day old daphnia in 50 cc. culture medium, and 25 cc. of filtrate No. 101 were added to a like number of daphnia in 75 cc. of culture medium (test solution No. 101A, $\frac{1}{4}\%$).

Time	No. 100 ($\frac{1}{2}\%$)	No. 100 ($\frac{1}{2}\%$)	No. 101A ($\frac{1}{4}\%$)
$\frac{1}{2}$ hour	18/32	10/40	20/30
1 "	30/20	25/25	25/25
$1\frac{1}{2}$ "	40/10	20/30
2 "	30/20	15/35	20/30
$2\frac{1}{2}$ "	14/36
3 "	20/30	2/48-5/45	15/35
$3\frac{1}{2}$ "	20/30	0/50	15/35
4 "	20/30	10/40
$4\frac{1}{2}$ "	8/42	10/40
5 "	5/45	10/40
$5\frac{1}{2}$ "	0/50	5/45-10/40

The results of experiment 2 have confirmed those of experiment 1. Assigning unity to lot No. 100, then the factor for lot No. 101 is greater than one and less than two.

3

In order to approximate the factor established in experiment 2, the following procedure was carried out. One per cent. filtrates from the two lots were made as previously described. Fifty cubic centimeters from filtrate No. 100 were added to fifty standardized ten day old daphnia in 50 cc. culture medium, 30 cc. of filtrate No. 101 were added to a like number of daphnia in 70 cc. of culture medium (101B, $\frac{3}{10}$ per cent.) and finally, 35 cc. of No. 101 filtrate to 65 cc. culture medium with the like number of daphnia (No. 101C, $\frac{7}{20}$ per cent.). A sudden change in weather raised the temperature from 24.5 degrees to 27 degrees C. during the experiment.

Time	No. 100 (1/2%)	No. 101B (3/10%)	No. 101C (7/20%)
1 hour	20/30	10/40	10/40
2 "	12/38	8/42	2/48
2 1/2 "	8/42	3/47	1/49-0/50
3 "	4/46-0/50	2/48-0/50	0/50, (all down quiescent)
3 1/2 "	3/47-0/50	1/49-0/50	
3 3/4 "	6 active in lower half	1 active in lower half	
4 "	all down, 4 not quiescent	all down and quiescent	
4 1/2 "	all down and quiescent		

In the time range of 3-3 1/2 hours, it appeared that No. 100 and No. 101B were fairly well matched. However, upon closer study it was apparent that No. 101B had a slightly greater effect on the test animals. The factor for a perfect match here would be 1.66. Actually the difference is slightly larger, hence the factor of 1.7 can be assigned with reasonable assurance.

Discussion

Biological standardization of drug powders, solid extracts, etc. whose activity is due to a complex rather than any one active agent is necessary to insure the uniform potency of the final preparation. It is obviously apparent that if the two lots of powdered *Veratrum viride* tested were extracted in accordance with the U. S. P. standards, the method of extraction alone could not guarantee the uniform potency of the preparations. The *Daphnia* method offers a rapid, inexpensive and accurate means of evaluating the activity of such substances which owe their activity to a complex, especially when the locomotion of the *daphnia* is visibly affected in their presence.

Summary

The *Daphnia* method for the evaluation of powders of *Veratrum* has been described. Two lots of *Veratrum viride* tested by this method has shown that one lot was 1.7 times more toxic than the other. The application of this test to other substances was briefly indicated.

Literature

- (1) Viehoveer, A., and Cohen, I.: Physiological Evaluation of *Veratrum Viride* and *V. Album*. I. Toxicity. *Am. J. Pharm.*, **111**, 3 (1939).
- (2) Viehoveer, A., and Cohen, I. The Responses of *Daphnia Magna* to Vitamin E. *Am. J. Pharm.*, **110**, 7 (1938).

EFFICIENCY OF BACTERICIDAL AGENTS IN DIFFERENT OINTMENT BASES

By Louis Gershenfeld and Russell E. Brillhart

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MANY new types of ointment bases are being made available. Investigation and comparison of these new and the old bases have been undertaken to study the efficiency of various bactericidal agents employing the different bases as vehicles.

Medicinal ointments depend upon diffusion and absorption, primarily, to produce the effects of the active therapeutic agents present. The inclusion of water in ointments has become an important factor as pointed out by Lesser (1), this resulting in a demand for bases that will carry large amounts of water or water soluble drugs.

The purport of this investigation was to compare the results produced by various new and old type ointment bases containing certain bactericidal agents, to determine whether there was a definite relationship between diffusion and the amount of water carried by the vehicle, and to extend the investigation on the new ointment bases, reported previously by one of us (2).

Procedure

Reagents Used

I—Ointment Bases

- | | | |
|--|---|-------------|
| (a)—Synthetic Wax Bases | } | Newer Bases |
| (b)—Oxycholesterin Bases | | |
| (c)—U. S. P. XI Bases | | |
| (d)—Benzoinated Lard Base | } | Older Bases |
| (e)—Petrolatum Base | | |
| (f)—2 per cent. Cholesterin added to (d) and (e) bases | | |

II—Bactericidal Agents

- (a)—Ammoniated Mercury (10 per cent.)
- (b)—Phenol (2 per cent.)
- (c)—Bichloride of Mercury (0.1 per cent.)

III—Formulae

The formulæ for the ointments as used for these tests are given in Tables A, B and C.

In every instance, in so far as possible, an attempt was made to employ a vanishing cream formula for the ointments except in the U. S. P. XI group, the Benzoinated Lard and Petrolatum groups.

Fifty grams of each ointment were prepared, including the bactericidal agents, the latter replacing water, gram for gram in each instance except in the control bases.

A 5 per cent. aqueous solution of phenol was prepared and 20 cc. of this solution were used in each 50 grams of phenol ointment made (this making a 2 per cent. phenol solution). A 1 per cent. aqueous solution of bichloride of mercury was prepared and 5 cc. of solution were used in each 50 grams of ointment prepared to give a 0.1 per cent. bichloride of mercury concentration. Ammoniated mercury was added as in the U. S. P. XI official method (3).

Technique Used

The Agar Plate and Agar Cup Plate Methods were employed in the tests (4), using *Staphylococcus aureus* as the test organism.

In making the cups, a modification was used in that a sterile sublimation ring was placed in the center of the plate and the agar was poured around it. After solidification, the ring was removed with a sterile forceps by a slight rotary motion and the center plug of agar was removed with a toothpick, producing a neat cup without cracking.

Three samples were tested in each case using one agar plate and two agar cup plates. The smears were made to have intimate peripheral contact by using a slightly warmed spatula or a sterile toothpick. The cups were filled advantageously by means of a sterile spatula or sterile toothpick.

TABLE A

BACTERICIDAL EFFICIENCY OF 10% AMMONIATED MERCURY OINTMENTS

I SYNTHETIC WAX GROUP		Inhibition Zone 3 tests each (all zones in mm.) C—Cup plate A—Agar plate		Sub-cultures made from center of inhibition zone	
Preparation					
(A)	Ammoniated Mercury 10%				
	Base 90%				
(Selzer comm. suggested U. S. P. vanishing cream)					
(1)	Glyceryl Monostearate 15. %	C	— 11	11.5	No growth
	Cetyl Alcohol 2.5%	C	— 13		No growth
	Diethylene Glycol 3.0%	A	— 10.5		No growth
	Dist. Water 79.5%				

TABLE A—Continued

Preparation		Inhibition Zone 3 tests each (all zones in mm.) C—Cup plate A—Agar plate		Sub-cultures made from center of inhibition zone	
(B)	Ammoniated Mercury Base	10% 90%			
	(2) Tegin P	3.5%			
	(3) Triethanolamine	0.7%			
	Glycerine	1.7%			
	Water	77.7%	C — 15 C — 16 A — 15	} 15.3	No growth No growth No growth
	Stearic Acid	13.4%			
	Mineral Oil	2.0%			
	(2) Iso-Lan	1.0%			
(C)	Ammoniated Mercury Base	10% 90%			
	(2) Tegin	12 %			
	Mineral Oil	2 %	C — 13	} 12	No growth
	Glycerin	5 %	C — 11		No growth
	Spermaceti	5 %	A — 12		No growth
	Water	76 %			
(D)	Ammoniated Mercury Base	10% 90%			
	(2) Tegacid	15 %			
	Glycerin	6 %	C — 12	} 11.7	No growth
	Spermaceti	5 %	C — 11		No growth
	Mineral Oil	4 %	A — 12		No growth
	Citric Acid	0.2%			
	Water	69.8%			
II					
OXYCHOLESTERIN BASE GROUP					
(E)	Ammoniated Mercury Base	10% 90%			
	(4) Falba	5 pts.			
	(1) Glyceryl Monostearate	10 pts.	C — 15	} 14	No growth
	Spermaceti	5 pts.	C — 14		No growth
	Glycerin	3 pts.	A — 13		No growth
	Water	80 pts.			
(F)	Ammoniated Mercury Base	10% 90%			
	(5) Lanaform	26 %			
	(Consists of Adeps Lan- ae, Beeswax, Peanut Oil, Cholesterin Phos- phate, Veg. Lecithin)		C — 11 C — 11 A — 8.5	} 10.2	No growth No growth No growth
	Water	74 %			

TABLE A—Continued

Preparation		Inhibition Zone 3 tests each (all zones in mm.) C—Cup plate A—Agar plate			Sub-cultures made from center of inhibition zone
(G)	Ammoniated Mercury Base	10% 90%			
	(6) Aquaphor	20 %			
	Mineral Oil	6 %	C — 10	} 10.3	No growth
	Lanolin	3 %	C — 12		No growth
	Glycerin	5 %	A — 9		No growth
	Water	66 %			
(H)	Ammoniated Mercury Base	10% 90%			
	(7) Aquaphil	22 %			
	Mineral Oil	6 %	C — 9	} 7.2	No growth
	Lanolin	3 %	C — 6		No growth
	Glycerin	5 %	A — 6.5		No growth
	Water	64 %			
III					
U. S. P. XI, and OLDER BASES (FATTY, ETC.)					
(I)	Ammoniated Mercury	10 %	C — 9	} 8	No growth
	(8) Benzoinated Lard (plain)		C — 8		No growth
		90 %	A — 7		No growth
(J)	Ammoniated Mercury	10 %	C — 8.5	} 7.7	No growth
	(8) Benzoinated Lard (plain)		C — 8.0		No growth
	(8) 2% Cholesterin	90 %	A — 6.5		No growth
(K)	U. S. P. XI				
	Wool Fat	5 %	C — 8.5	} 6.5	No growth
	White Wax	5 %	A — 5.5		No growth
	Ammoniated Mercury	10 %	A — 5.5		No growth
	White Petrolatum				
(L)	Ammoniated Mercury	10 %	C — 6.5	} 6	No growth
	White Petrolatum		C — 6.0		No growth
	(8) 2% Cholesterin	90 %	A — 5.5		No growth

See Footnotes under Table B.

Control tests of the bases themselves, without the bactericidal agents were made and produced no inhibitory zone in every instance.

Sub-cultures were made for each inhibition zone obtained from the center of the zone, and were negative in all cases.

TABLE B
BACTERICIDAL EFFICIENCY OF 2% PHENOL OINTMENTS

IV SYNTHETIC WAX GROUP		Inhibition Zone 3 tests each (all zones in mm.) C—Cup plate A—Agar plate		Sub-cultures made from center of inhibition zone	
Preparation					
(A)	Phenol Base	2% 98%			
	(Selzer comm. suggested U. S. P. vanishing cream)				
	(1) Glyceryl Monostearate	15. %	A — 2 A — 2 C — 2.5	2.2	No growth No growth No growth
	Cetyl Alcohol	2.5%			
	Diethylene Glycol	3.0%			
	Dist. Water	79.5%			
(B)	Phenol Base	2% 98%			
	(2) Tegin P	3.5%	C — 1.5 C — 1.5 *A — 1.5	1.5	No growth No growth No growth *Plate broke
	(3) Triethanolamine	0.7%			
	Glycerin	1.7%			
	Water	77.7%			
	Stearic Acid	13.4%			
	Mineral Oil	2.0%			
	(2) Iso-Lan	1.0%			
(C)	Phenol Base	2% 98%			
	Tegin	12 %	C — 5 C — 5 A — 5	5	No growth No growth No growth
	Mineral Oil	2 %			
	Glycerin	5 %			
	Spermaceti	5 %			
	Water	76 %			
(D)	Phenol Base	2% 98%			
	Tegacid	15 %	C — 2 C — 2 A — 2	2	No growth No growth No growth
	Glycerin	6 %			
	Spermaceti	5 %			
	Mineral Oil	4 %			
	Citric Acid	0.2%			
	Water	69.8%			

TABLE B—Continued

V					
OXYCHOLESTERIN BASE GROUP					
Preparation		Inhibition Zone 3 tests each (all zones in mm.) C—Cup plate A—Agar plate		Sub-cultures made from center of inhibition zone	
(E)	Phenol Base	2% 98%			
	(4) Falba	5 pts.			
	(1) Glyceryl Monostearate	10 pts.	C — 3	} 2.7	No growth
	Spermaceti	5 pts.	C — 3		No growth
	Glycerin	3 pts.	A — 2		No growth
	Water	80 pts.			
(F)	Phenol Base	2% 98%			
	(5) Lanaform	26 %	C — 4	} 3.8	No growth
	(Consists of Adeps Lanae, Beeswax, Peanut Oil, Cholesterin Phosphate, Veg. Lecithin)		C — 4		No growth
			A — 3.5		No growth
	Water	74 %			
(G)	Phenol Base	2% 98%			
	(6) Aquaphor	20 %	C — 0	} 0	Growth
	Mineral Oil	6 %	C — 0		Growth
	Lanolin	3 %	A — 0		Growth
	Glycerin	5 %			
	Water	66 %			
(H)	Phenol Base	2% 98%			
	(7) Aquaphil	22 %	C — 1	} 1.3	No growth
	Mineral Oil	6 %	C — 2		No growth
	Lanolin	3 %	A — 1		No growth
	Glycerin	5 %			
	Water	64 %			

TABLE B—Continued

VI

U. S. P. XI AND OLDER BASES
(FATTY, ETC.)

U. S. P. XI AND OLDER BASES (FATTY, ETC.)		Inhibition Zone 3 tests each (all zones in mm.) C—Cup plate A—Agar plate		Sub-cultures made from center of inhibition zone	
Preparation					
(I)	Phenol	2 %	C — 0.5	} 0.5	Growth Growth Growth
	(8) Benzoinated Lard		A — 0.5		
	(plain)	98 %	A — 0.5		
<hr/>					
(J)	Phenol	2 %	C — 0	} 0	Growth Growth Growth
	(8) Benzoinated Lard		C — 0		
	(plain)	98 %	A — 0		
	(8) 2% Cholesterin				
<hr/>					
(K)	U. S. P. XI				
	Yellow Wax	5 %	C — 0	} 0	Growth Growth Growth
	Phenol	2 %	A — 0		
	Petrolatum	93 %	A — 0		
<hr/>					
(L)	Phenol	2 %	C — 0	} 0	Growth Growth Growth
	White Petrolatum		C — 0		
	(8) 2% Cholesterin	98 %	A — 0		

Key for Numbers Preceding Formulae in Tables

(1) Brand of Glyceryl Monostearate. Distributed by Glyco Products Co., Inc., 148 Lafayette St., New York, N. Y.

(2) (a) Tegin P, brand of Propylene Glycol Monostearate; (b) Tegin, brand of Glyceryl Monostearate; (c) Tegacid, prepared from Glyceryl Monostearate (Tegin); (d) Iso-Lan. Oxycholesterin product. All distributed by The Goldschmidt Corporation, 153 Waverly Place, New York, N. Y.

(3) Triethanolamine. Distributed by Carbide and Carbon Chemicals Corp., New York, N. Y.

(4) Falba (Oxycholesterin Absorption Base). Distributed by Pfaltz & Bauer, Inc., Empire State Building, New York, N. Y.

(5) Lanaform (Oxycholesterin Absorption Base). Distributed by The Doak Company, Cleveland, Ohio.

(6) Aquaphor (an Oxycholesterin Absorption Base). Distributed by Duke Laboratories, Inc., 4610 Eleventh Street, Long Island City, N. Y.

(7) Isco-Aquaphil (an Oxycholesterin Absorption Base). Distributed by Innis, Speiden & Company, 117 Liberty Street, New York, N. Y.

(8) Products of Wilson & Company, Laboratories, Chicago, Ill.

TABLE C

BACTERICIDAL EFFICIENCY OF 0.1% BICHLORIDE OF MERCURY

VII

SYNTHETIC WAX GROUP

Preparation		Inhibition Zone 3 tests each (all zones in mm.) C—Cup plate A—Agar plate		Sub-cultures made from center of inhibition zone
(A)	HgCl ₂ Base	0.1% 99.9%		
	(Selzer Comm. suggested U. S. P. vanishing cream)			
	(1) Glyceryl Monostearate	15. %	A — 6	} 6.8 No growth No growth No growth
	Cetyl Alcohol	2.5%	C — 6.5	
	Diethylene Glycol	3.0%	C — 8	
	Dist. Water	79.5%		
<hr/>				
(B)	HgCl ₂ Base	0.1% 99.9%		
	(2) Tegin P	3.5%		
	(3) Triethanolamine	0.7%		
	Glycerin	1.7%	C — 11	} 10.7 No growth No growth No growth
	Water	77.7%	C — 11	
	Stearic Acid	13.4%	A — 10	
	Mineral Oil	2.0%		
	(2) Iso-Lan	1.0%		
<hr/>				
(C)	HgCl ₂ Base	0.1% 99.9%		
	(2) Tegin	12 %		
	Mineral Oil	2 %	C — 9	} 8.3 No growth No growth No growth
	Glycerin	5 %	C — 8	
	Spermaceti	5 %	A — 8	
	Water	76 %		
<hr/>				
(D)	HgCl ₂ Base	0.1% 99.9%		
	(2) Tegacid	15 %		
	Glycerin	6 %	C — 9	} 9.7 No growth No growth No growth
	Spermaceti	5 %	C — 10	
	Mineral Oil	4 %	A — 10	
	Citric Acid	0.2%		
	Water	69.8%		

TABLE C—Continued

VIII						
OXYCHOLESTERIN BASE GROUP						
Preparation		Inhibition Zone 3 tests each (all zones in mm.) C—Cup plate A—Agar plate		Sub-cultures made from center of inhibition zone		
(E)	HgCl ₂ 0.1% Base 99.9%					
(4)	Falba 5 pts.					
(1)	Glyceryl Monostearate 10 pts.	C — 14	} 12.3	No growth		
	Spermaceti 5 pts.	C — 12		No growth		
	Glycerin 3 pts.	A — 11		No growth		
	Water 80 pts.					
<hr/>						
(F)	HgCl ₂ 0.1% Base 99.9%					
(5)	Lanaform 26 %					
	(Consists of Adeps Lan- ae, Beeswax, Peanut Oil, Cholesterin Phos- phate, Veg. Lecithin)	C — 8	} 6.8	No growth		
		C — 7.5		No growth		
	Water 74 %	A — 5		No growth		
<hr/>						
(G)	HgCl ₂ 0.1% Base 99.9%					
(6)	Aquaphor 20 %					
	Mineral Oil 6 %	C — 11	} 11.	No growth		
	Lanolin 3 %	A — 9		No growth		
	Glycerin 5 %	A — 10		No growth		
	Water 66 %					
<hr/>						
(H)	HgCl ₂ 0.1% Base 99.9%					
(7)	Aquaphil 22 %	C — 8	} 8.5	No growth		
	Mineral Oil 6 %	C — 10.5		No growth		
	Lanolin 3 %	A — 7		No growth		
	Glycerin 5 %					
	Water 64 %					

TABLE C—Continued

IX U. S. P. XI AND OLDER BASES (FATTY, ETC.)		Inhibition Zone 3 tests each (all zones in mm.) C—Cup plate A—Agar plate		Sub-cultures made from center of inhibition zone	
Preparation					
(I)	HgCl ₂	0.1%	C — 6.5	} 7.2	No growth
	(8) Benzoinated Lard		C — 7		No growth
	(plain)	99.9%	A — 8		No growth
(J)	HgCl ₂	0.1%	C — 9	} 8.5	No growth
	(8) Benzoinated Lard (plain)		C — 9		No growth
	(8) 2% Cholesterin	99.9%	A — 7.5		No growth
(K)	Using U. S. P. XI. Simple Ointment to correspond with U. S. P. Ammoniated Mercury and U. S. P. Phenol				
	Mercury Bichloride	0.10%	C — 8	} 7.8	No growth
	Yellow Wax	5.00%	A — 7.5		No growth
	Petrolatum	94.90%	A — 7.8		No growth
(L)	HgCl ₂	0.1%	C — 4	} 4.3	No growth
	White Petrolatum		C — 5		No growth
	(8) 2% Cholesterin	99.9%	A — 4		No growth

See Footnotes under Table B.

Observations

See Tables A, B and C

The following base groups are arranged according to the size of the Inhibition Zones produced—(a) group giving the greatest in width decreasing to (e) the smallest.

(a)—Synthetic Wax Base Group

(b)—Oxycholesterin Base Group

(c)—Benzoinated Lard Group

(d)—U. S. P. XI Base Group

(e)—Petrolatum Base Group

There was a direct relation in the Inhibition Zones formed within each group, in that the more water the ointment contained the greater was its Inhibition Zone. This relation varied slightly in the Synthetic Wax and Oxycholesterin groups, depending somewhat on variation of ingredients and probably on physical factors.

Comparing the older and the U. S. P. XI bases with the newer bases, a wide variation was noted in that the Inhibition Zones of the older types and U. S. P. XI bases were considerably smaller. This may be explained by the fact that the newer bases hold much more water due to the presence of emulsifiers, and that these emulsifiers efficiently lower interfacial tension and permit diffusion more readily through the agar. The water in turn carried the medicinal agent with it producing a larger Inhibitory Zone in practically a direct ratio.

One of the Oxycholesterin Bases (Falba) gave a greater Inhibitory Zone than the others in its own group and even exceeded some of the Synthetic Wax group. It is to be noted that this particular ointment prepared with "Falba" contained a high percentage of water and in addition there was added Glyceryl Monostearate (9.8 per cent.), an efficient emulsifier and synthetic wax used in the wax group. This probably accounts for its (Falba's) efficiency in this test.

The addition of 2 per cent. cholesterin did not improve the older bases so far as increasing the Inhibition Zone.

Upon reading Inhibition Zones, it was noted that the boundary of the Inhibition Zone was not so distinct but faded off gradually in those ointments containing Glyceryl Monostearate, apparently due to a lessening of diffusion. In the other ointments there was a very distinct boundary zone probably due to the agent being bound more firmly.

The Bactericidal Agents used were variable among themselves, as is to be expected:

Ammoniated Mercury (10 per cent.)—Produced the best results

Bichloride of Mercury (0.1 per cent.)—Next best results

Phenol (2 per cent.)—The poorest results

The following table consists of the AVERAGE Inhibition Zone for each group of bases and for each bactericidal agent.

Base groups	Amm. Hg. (10%)	HgCl ₂ (0.1%)	Phenol (2%)
Synthetic Wax	12.6 mm.	8.9 mm.	2.5 mm.
Oxycholesterin	10.4 mm.	9.7 mm.	2.0 mm.
U. S. P. XI and Older Types	7.0 mm.	7.0 mm.	0.125 mm.

(a)—It is evident from the foregoing and the results as seen in tables A, B and C that the bactericidal agents produced better results when incorporated in the newer bases as compared with the older and U. S. P. XI bases.

(b)—Phenol (2 per cent.) produced small inhibition zones with the newer base groups while with the older base groups the zones were negligible to none.

It is self-evident from the tables and discussion that the present U. S. P. bases are not efficient in terms of Inhibition Zones in that they retard diffusion of the agents added. On the basis of these and previous (2) findings, we recommend the newer bases as vehicles for bactericidal agents because of:

(1)—Their efficiency over the present official ones as interpreted in terms of inhibition zones.

(2)—Their ease of preparation and water holding ability.

The rate and extent of diffusion of the bases were evidently influenced to some degree by characteristics such as surface tension, pH, adhesion, cohesion, solubility, melting point, colloidal properties, electrical charge, etc.

The Diffusion and Inhibition Zones on a series of the plates remained constant after several months had elapsed. This was not a variable in itself to be considered.

The Agar Cup Plate produced slightly higher readings as compared with the Agar Plate Method due in part to better ointment agar contact and therefore more ease of diffusion.

Agar Cup Plates were much easier and uniform to make measurements from plus the ease of depositing ointment in a definite area.

Of the older bases Benzoinated Lard produced slightly larger Inhibition Zones than the U. S. P. XI and Petrolatum bases.

Summary

A report is given on an investigation of 48 ointments checked by the F. D. A. Agar Plate and Agar Cup Plate Techniques.

In order to compare newer and older bases, these ointments were grouped for study as follows:

Synthetic Wax group—4 different bases	}	Newer Ointment Types
Oxycholesterin group—4 different bases		Vanishing Cream Formula, Greaseless
U. S. P. XI	}	Older Ointment Types
and		
Older Bases group—4 different bases	}	

Four ointments were made for each base used:

- 1—To contain Ammoniated Mercury (10 per cent.)
- 2—To contain Phenol (2 per cent.)
- 3—To contain Bichloride of Mercury (0.1 per cent.)
- 4—Ointment without agent as control

Each of these ointments was checked three times by the F. D. A. Agar Plate and Agar Cup Plate Methods and readings recorded as given in the Tables.

Conclusion

The tests indicated that Bactericidal Agents used in the newer water-miscible ointment bases produced greater bacteriostatic action as revealed by the production of inhibition zones than in the older type of bases when tested by the F. D. A. Agar Plate and Agar Cup Plate techniques. We again repeat the recommendation made by one of us more than six years ago (2):

"We recommend that the U. S. P. or N. F. arrange to include such formulas in their next revision, and we further recommend that the Pharmacopœial Revision Committee arrange for a thorough study of these water soluble ointment bases as they appear to be more satisfactory vehicles for bactericidal agents than other ointment bases."

Acknowledgment

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HAVE A SMOKE?

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Falls Church, Va.

THE American Indian was always a pretty up-to-date fellow. He held conferences and he smoked while conferring. Fortunately for the nonsmokers he held them outdoors. Today the nonsmokers, if any, are mentally dead or unconscious for days after a conference, a condition induced by inhaling the exhaled, smoke-laden breath of others.

By 1931 it was estimated that the inhabitants of the United States smoked 119,653,000,000 cigarettes a year, of which women of 35 or less were said to have consumed 16,940,000,000. It looks as if the Indians really started something. (1)

The ancient Romans smoked, according to Pliny, but not for pleasure—and besides, it wasn't tobacco. They smoked to cure diseases. But Columbus found the American Indians not only smoking but chewing and sniffing tobacco as well.

Legend has it that Sir Walter Raleigh introduced the habit of using the weed in England and it gripped the Elizabethans quickly. It spread despite all efforts to combat it from the frowns of priests to lashings with knouts. Soon man, woman and child indulged. The French scholar Jean Nicot achieved a certain immortality after his death in 1600 by bequeathing part of his name to nicotine.

Today two sure-fire news stories recur periodically: 1, The one about the cigar-smoking tot; 2, the one about the centenarian who achieved great age because he did or did not use tobacco freely.

It is commonly held that such excessive use of tobacco as occurs all about us must be bad for the health, but there is strangely little proof of that all told. Does smoking injure health, and, if so, how?

A rather careful study made in 1929 of 150 adult male smokers and the same number of nonsmokers (2) indicated this:

Smoking had little effect upon the blood pressure other than perhaps temporarily to reduce it. Other work has since confirmed this. Smoking does not tend to decrease weight nor to bring on angina pectoris. There is no specific toxic effect because tolerance is so soon established. Melancholy tales about the extreme ill effects of smoking upon women and their babes are largely mythical.

The marked congestion of the pharynx, characteristic of the habitual smoker, is almost the sole ill effect of the habit.

Athletes are usually cautioned not to smoke. Some work reported in 1931 (3) indicated that such use of tobacco did have a little adverse effect on endurance. At least nonsmokers performed better than smokers in a three-mile cross-country run, but no effort was made to study the physiques and constitutions of men in each classification.

Possibly the nonsmokers were just born better. At least further work that appeared in 1932 (4) indicated that heavy smoking for several days had no bad effect on the wind during mild and moderately severe exercise. "Heavy smoking" meant twenty cigarettes daily.

It has been held by some doctors that the tar in cigarette smoke contains an irritant substance that could account for lung cancer. But other doctors deny this flatly, insofar as smoke is concerned. For it is generally agreed that mouth cancer is unduly prevalent among smokers. On the other hand, that may not implicate tobacco. The mechanical irritation of holding any solid object like pipe or cigarette holder in the mouth might alone be responsible.

In general physicians hold that smoking produces no apparent injury in sound individuals.

Patients with stomach or intestinal ulcer are usually told not to smoke on the theory that smoking causes or irritates the ulcers. But recent careful study (6) indicates that there is lack of sound evidence here.

In other words, it was common for doctors to record that sufferers from ulcer were "habitual smokers." But when fifty victims of duodenal ulcer were closely compared with four hundred normals it was found that the latter smoked as much on average as the former. This was no direct case of cause and effect.

In March, 1939, it was announced that smoking stimulates the flow of saliva and stops hunger contractions dead by a sort of reflex action. It does not affect the emptying time of the stomach nor increase gastric acidity. This was true of both normals and sufferers from ulcer. (7)

In general smoking does not affect either the output of the digestive juices nor the general process of digestion. It probably is a slight aid in constipation. Above all, it pervades the habitual user with a sense of pleasurable repose, a sort of digestion-promoting euphoria.

Furthermore, definite evidence is still lacking to prove even that stomach ulcer patients should not smoke. They should be cautioned to be moderate. But, according to this work appearing in 1939, doctors have no ground to forbid them their solacing weed altogether.

It is well known that smoking affects the action of the heart, the circulation, and the bodily temperature. Cigarette smoking causes a temperature drop in the tips of the toes and fingers ranging from 5 to 15 degrees Fahrenheit, depending on the individual. Denicotinized and mentholated cigarettes have the same effect as ordinary ones.(8)

Nicotine is usually singled out as the drug in tobacco potent to produce these effects. As it is so largely destroyed in dry tobacco, the moisture content of a tobacco rather than its original nicotine content is the thing that determines its possible harmfulness.

Then it must always be remembered how much individuals differ. Some people exhibit marked toxic effects after smoking only one cigarette. What is moderation for one would be harmful excess for another.

When subjects were tested after smoking three-fourths of a cigarette of any of several popular brands, the third finger of the left hand of some showed a temperature drop of 4 or 5 degrees. But in others it went up 8 degrees and in still others there was no temperature change at all.(9)

But, though nicotine is usually blamed, more research must be done on the toxic effects of tobacco smoke before that is absolutely certain. Nicotine is known, however, to stimulate the sympathetic nervous system, and it should always be remembered that so-called "denicotinized" cigarettes contain at least one-third as much of the drug as do ordinary ones.

Contrary to advertising myths, evidence is lacking that the "acidity" of tobacco smoke has any relationship to the health of the smoker even as regards throat irritation. Furthermore, tests have shown that popular brands of cigarettes differ from one another no more in acidity than do varying specimens of the same brand.(10)

Raymond Pearl's studies did indicate that even moderate smoking decreased the life span, but the smoker perhaps packs more pleasure into less years. He studied an unselected lot except for their use of tobacco. Heavy smokers had a much poorer life expectancy than heavy drinkers and even those who indulged moderately impaired their life span.

But here is something quite new that seems rather important. It has been observed by both doctors and laymen that smoking makes many individuals "nervous." (8) The extent of this effect depends upon the fatigue and nutrition states as well as upon the emotions and inherited neurovascular balance of the individual.

Immoderate or chain smokers often demonstrate this state of tension by discarding frequent long butts. Since nicotine is so powerful a drug it is reasonable to suppose that it causes this nervousness by its effects on the sympathetic nerves, the adrenal gland, and the level of sugar in the blood.

Any agency at all that affects our ability to use our bodily stores of sugar for energy, or to fight off infections, assumes importance. Our very ability to think depends on our sugar metabolism. Hence heavy injections of insulin which deplete the body's sugar supply interfere with the normal oxidative processes going on in the brain. So insulin is used in what is called "shock therapy" for certain forms of psychosis.

Anything at all that impedes those sugar-oxidative processes will tend to produce nervousness, fatigue feelings, lack of coordination, impaired memory, judgment or insight and—in the extreme, coma or mental disorder. High altitudes where oxygen is rare, lack of vitamin B₁, certain poisons and narcotic drugs all tend to produce such disturbance.

These things deprive the brain and the nervous system of the sugar glucose, or of the ability to oxidize, or burn, it for energy. Then nerve and brain functioning, and the power to fight off infections also, are both impaired.

In late 1938 a physician reported on six cases of extreme fatigue in which all forms of treatment proved unavailing until he told his patients to stop smoking. (11) Then their fatigue vanished. Some were male, some female, and their daily cigarette consumption had varied from ten to forty-five coffin nails each.

Cigarette smoking was found to produce an increase in the heart rate and other changes in the electrocardiogram. Both ordinary and denicotinized cigarettes produced this effect and filter holders did nothing to decrease it.

When the smoke from two-thirds of an ordinary cigarette is inhaled the smoker gets 3.33 milligrams of nicotine. Even if 70 per cent. of the nicotine has been removed he still gets a milligram of the powerful drug and that is sufficient to affect him. That is one-

thousandth of a gram, which is, in turn, about one-twenty-eighth of an ounce.

Smoking even one cigarette increases the quantity of sugar in the blood also. It does this by somehow effecting the break-down of glycogen, the starchlike source of carbohydrates for energy that we store in our muscles and liver. When it is depleted we have less potential energy to draw upon, hence smoking causes a direct energy loss.

Hence chronic smoking by affecting the nerves, heart, circulatory system, adrenal gland, and blood sugar level can produce fatigue. Work published nearly twenty years ago indicated that brain workers who smoked had less ability to respond to an increasing work load as the day wore on than did nonsmokers.

The fact that smoking affected the blood sugar level was brought to the attention of the general public about 1934 (12), but it was not just discovered then. Some workers have denied this effect (13), but in general it stands confirmed. The blood sugar does rise.

This was immediately seized upon by cigarette advertisers who had steadily ignored such other findings as that smoking reduced the temperature of the extremities and caused adverse heart and circulatory changes.

Consumers were told that there was now "scientific confirmation" of the "energizing effects" of smoking. Smoke! and up goes your energy curve "without jangling your nerves." Oddly enough only one popular brand of cigarettes was advertised thus to "drive away fatigue and irritation," though any brand would do this under laboratory control.

But in reality there was no such action. This was plain distortion of scientific findings and an unwarranted inference from fact. True enough, when a cigarette is smoked, hunger is eliminated and the blood sugar rises.

But Carlson and Lewis showed in 1914 that nicotine stopped the stomach's hunger contractions, though the hunger might still be there unfelt. Furthermore, the rise in blood sugar always indicates depletion of the important energy stores of glycogen, and it forms part of a general protective mechanism the body uses to defend itself against the insidious effects of strong drugs and virulent germs. (14)

Even in 1912 it was known that injections of nicotine would increase an animal's secretion of adrenalin. In 1925 it was known that this was accompanied by a rise in the blood sugar. In 1928, six years before the public announcement of the "discovery" in 1934, it

was known that smoking a cigarette would produce the same result in human beings that nicotine injections produced in animals.

In 1931 an extensive monograph appeared to show that glycogen stored in the liver and muscles was released by smoking. By acting on the adrenal gland and releasing the sugar a smoke does dispel fatigue and irritation, but at the expense of an important bodily source of energy. One does not get "harmless" temporary relief from fatigue by smoking. Instead one sets in motion an important defense mechanism that should be used only in proper emergencies.

There is a definite increase in blood sugar following the administration of many powerful drugs. There is a rise also in a variety of infections ranging from influenza to syphilis, as well as in cancer, bad burns, asphyxia, and hemorrhage. Rats lacking adrenal glands, on which nicotine acts, are ten to twenty times more sensitive to morphine poisoning than are normal rats. If injected with adrenalin they also fight off infections better.

The adrenalin raises the blood sugar level. There you have the entire response: Action of a drug like nicotine on the sympathetic nerves; action of the nerves to increase the secretion of adrenalin; action of the adrenalin to cause a rise in the blood sugar content. At the same time the respiratory quotient rises; metabolism and sugar oxidation speed up.

Sugar is burned for energy. The organism can use the energy either to repel a germ attack (as by fever) or to combat a poison. The sympathetic nervous system is the electric burglar alarm that sets off the whole mechanism. The shift in blood sugar argues no availability of increased muscular energy. It argues instead reduction in the muscle and liver energy stores of glycogen.

When the blood sugar is high an animal tends to be lethargic, as we are after meals or when fighting an infection. In rage, fear, or pain the blood sugar rises and we clear decks for supreme physical exertion. But when we are toxic or infected the protective mechanism acts to lull us and thus avoid any increase in toxins by the further breakdown of our tissues and energy stores.

When sugar is mobilized the respiratory action increases—as in rage or in fever—and we are ready to fight off either a dangerous beast or a toxic infection. Glycogen provides the necessary energy fuel in either case. Tobacco, like opium or influenza, sets off this mechanism. The appearance of hunger and fatigue is delayed.

Obviously the constant use of tobacco touches this mechanism off repeatedly. Every time a cigarette is smoked that can occur. Nat-

urally this can produce extreme fatigue in some individuals. In any case the ultimate result of smoking cannot be regarded as completely harmless.

This does not mean that everyone should quit smoking. It means that the blood-sugar rise that accompanies the smoke does not indicate an increase in available muscular energy. Instead it is more like whipping a tired horse. The "lift" is really a handicap. Nature seeks to counteract it by setting her protective mechanism in action.

Finally some folk manage completely to use up their energy stores of glycogen. They get chronically tired. A dozen or less cigarettes daily may do that for some individuals. If you smoke and also suffer from fatigue from an unassigned cause you might try quitting to see what would happen.

In a broad way it cannot be said, however, that smoking within moderation has any marked deleterious effects on people in sound health. Undoubtedly the pleasure so derived, and the sense of repose, overbalances the possible harm.

On the other hand, it might be just as well if smokers would remember that nonsmokers find the habit offensive in too close proximity. This arises from no etiolated moral squeamishness, but simply from the fact that any strong odor tends not to be disagreeable to those constantly exposed to it, but may be very offensive to others.

Those who do not smoke are rather too often compelled to inhale the exhalations of those who do. A certain modicum of courtesy seems indicated here—at least until the last half dozen nonsmokers die off or succumb to the weed.

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ABSTRACTS FROM AND REVIEWS OF THE LITERATURE OF THE SCIENCES SUPPORTING PUBLIC HEALTH

The Determination of the Oil Content of Emulsion of Cod Liver Oil. W. F. Kunkle. Report on Emulsions. *J. A. O. A. C.* 22, 739, (1939). The continuation of the study reported in the *J. A. O. A. C.* 21, 67 (1938) is described. The Soxhlet extraction with chloroform and with powdered pumice as a "spreader" was found to be undependable for three reasons namely (1) material was extracted when no oil was present, (2) the weight of the oil was found to increase due to a long period of refluxing and (3) low recovery.

The use of various "spreaders" was tried, namely, powdered pumice, small pieces of filter paper, filter-cel, sodium chloride, magnesium oxide, crystalline calcium carbonate and finely powdered calcium carbonate. Enough of the spreader was used with the emulsion to give practically a dry mixture in the preparation for extraction of the oil with chloroform.

Typical results for recovery of cod liver oil from an emulsion by extraction with chloroform and the use of various spreaders were: powdered pumice 99.8 per cent., filter paper 99.0-100.1 per cent., and filter-cel 100.1-100.8 per cent. Powdered pumice retains a comparatively large volume of chloroform and therefore a large volume of the solvent is necessary for extraction and washing; filter paper tends to form large masses which may in some cases cause troublesome and incomplete extraction; filter-cel was found to contain some chloroform soluble material which may account for the high results obtained. When this soluble material from filter-cel is removed prior to its use it is preferred next to finely powdered calcium carbonate which is first choice.

The drying period of 10 minutes on the steam bath with a current of air followed by 5 minutes at 100° C. to remove the chloroform as proposed in the method is well within the safe limits to avoid an increase in weight through absorption of oxygen.

Collaborative results using the proposed method were in good agreement.

L. F. T.

The Prevention of Carotene Absorption by Liquid Petrolatum. A. C. Curtis and R. S. Ballmer. *J. A. M. A.* 113, 1785 (1939). It has previously been shown that when rats were fed diets supplying the provitamin carotene, vitamin A deficiencies developed if liquid petrolatum was added to the diets in amounts comparable to the accepted dosage for human beings. Dutcher, Harris, Hartzler and Guerrant (*J. Nutrition* 8, 269 (1934)) have reported experiments showing that the carotene of a mixture of carotene and liquid petrolatum was not utilized when fed to animals but that the vitamin A of a carotene free cod liver oil concentrate mixed with liquid petrolatum was absorbed quite readily from the gastrointestinal tract.

Because many human beings obtain much of their vitamin A by conversion of the provitamin carotene into vitamin A and in view of the frequency that one of the many preparations of liquid petrolatum is prescribed for the relief of constipation or as a substitute for fat in a reducing diet regimen, the authors have determined whether a 65 and 80 per cent. emulsion of liquid petrolatum would have the same effect on removing carotene from the food of the gastrointestinal tract as plain liquid petrolatum. They also have investigated whether liquid petrolatum saturated with carotene both at room and body temperature would protect the carotene contained in the food of the gastrointestinal tract.

The results show that the emulsions taken in amounts of 20 cc. three times a day before meals or 20 cc. twice a day before the morning and evening meals interfered with the transportation of carotene across the epithelium of the intestine. Liquid petrolatum saturated with carotene at room temperature (0.26 per cent.) and taken in similar amounts still interfered with carotene absorption but when saturated at body temperature (0.28 per cent.) the blood carotene levels remained constant or increased slightly. The emulsions produced the same effect as unemulsified oil.

L. F. T.

The Experimental Treatment of Pinworm Infection. W. W. Wright, F. J. Brady and J. Bozicevich. *Pub. Health Rep.* 54, 2005

(1939). This paper is one of a series which reports the results of experiments designed to develop a satisfactory treatment for oxyuriasis.

The difficulty of eradicating pinworm infection is reflected by the many methods recommended in the literature for the treatment of this condition. Wright and Cram have shown that pinworm infection is usually a familial condition involving several or all members of the family. In view of this fact it appears futile from a control standpoint to treat some but not all infected individuals in a household, since treated individuals usually become reinfected promptly through ova scattered by nontreated individuals. Consequently, the authors in this study carried out diagnostic tests on all members of each family represented and all infected individuals treated simultaneously.

Twenty cases were treated with santonin in a single dose daily over a period of 10 days. Nine of these were positive and 11 were negative on post treatment examination. Some of the negative cases did not furnish a sufficient number of post treatment swabs and, consequently, the efficacy is probably at the rate of less than 50 per cent.

Eighteen of 27 cases treated with varying number of enemas consisting of hexylresorcinol in a dilution of 1:2000 in water were negative on post-treatment examination. Some of the positive patients received an inadequate number of enemas. The results indicate that such enemas are of considerable value in the treatment of pinworm infections. Ten enemas spaced over a period of 3 weeks constitute the minimum number necessary to eradicate the infection and some cases required more prolonged treatment.

Hexylresorcinol administered orally in the form of Caprokol pills does not constitute effective treatment.

Some of the anal ointments recommended in the medical literature appear to be of value in helping to allay the pruritis occasioned by the migration of gravid female pinworms but they are of little or no aid in the control of pinworm infections.

Non-medicated enemas, including soapsuds and saline enemas, are of advantage in infants and young children. Satisfactory results are not obtained however unless they are given every other night for at least 3 to 4 weeks.

L. F. T.

Recovery of the Virus of Poliomyelitis From the Stools of Healthy Contacts in an Institutional Outbreak. S. D. Kramer, A. G. Gilliam and J. G. Molner. *Public Health Rep.* 54. Since the times of Caverly and more particularly of Wickman a large mass of circumstantial evidence has been accumulated in support of the view that the poliomyelitis virus is widely distributed. These data are fairly consistent with the inference that in only a portion of those infected does the infection reach the level of clinical recognition.

The virus of poliomyelitis has been recovered from the upper respiratory and gastro-intestinal tracts of frank cases of the disease and from convalescents with sufficient frequency to establish the fact the virus may find egress from the human body through these channels. The virus has furthermore been recovered from the upper respiratory tract in instances of minor illnesses associated with frank cases of the disease.

There has been little effort expended to recover the virus from apparently healthy children and adults. Only three well defined instances of such successful attempts have been recorded in the literature. Inasmuch as in outbreaks of poliomyelitis carefully studied epidemiologically only 20 to 30 per cent. of cases give evidence of prior direct or indirect association with cases and suspected cases of the disease the virus is obviously spread from concealed sources. If these sources are human, and if transfer of infection is by human contact, then the concealed sources which might be either mild illnesses or healthy carriers must either outnumber clinically recognizable cases or must in some other manner be more effective in spreading infection than in definite cases.

The authors utilized an outbreak of poliomyelitis in a children's home in Detroit for a careful study of the presence of virus in well persons. At the time of the outbreak 34 children were in the home. In a group of 20 infants and preschool children from 2 months to 5 years of age, 1 fatal and 4 non-paralytic cases of poliomyelitis occurred. The virus was recovered from the stools of 3 out of 12 healthy children, contacts of these cases, and from an additional 2 out of 3 children who had had fevers of 24-48 hours duration. Thus including the 5 clinical infections 10 of the 20 children harbored poliomyelitis virus at some time in the 30 day study period. Virus was also recovered from the stool of one healthy adult out of specimens secured from eight adult attendants of the children. This individual,

the day nurse, in charge of the infant and preschool group was undoubtedly more continuously and intimately associated with them than was any other adult.

In two children virus was again recovered from stools taken 19 days after the first positive stools were obtained from them. Thus counting from the date of onset of the first case to the date of collection of the last positive stool the minimum limit in time in which the virus might have been present in some member of the group was 30 days. No case of poliomyelitis occurred in the children under 1 year of age but the stools of 3 out of 5 in this group yielded virus.

The facts developed in this institutional outbreak are consistent with a theory of transfer of infection by direct personal contact. Although they do not conclusively prove this or any other mode of spread they do offer corroborative evidence of the concept that the virus of poliomyelitis is usually spread throughout the general population by the agency of healthy carriers.

L. F. T.

The French Official Method for the Determination of Fat in Products Containing Only Small Amounts. E. A. M. Bradford. *Analyst* 64, 817 (1939). The French method as described in the *Service de la Repression des Fraudes* is not readily accessible in this country the author has translated this method which he claims to be superior to the usual methods of extraction.

FLOURS, BREADS, PASTRIES, EDIBLE PASTES, GROATS AND RASPIINGS.

Fatty substances.—The determination is made on 5 g. of flour weighed on a small scoop of silver-foil.

Apparatus.—A glass tube of the following dimensions is required: length, 24 cm.; external diameter, 19 mm. One end of the tube is drawn out so as to measure at the extreme tip not more than 6 mm. in diameter. The other end is widened to facilitate the introduction of the sample.

Method.—A small ball of absorbent cotton-wool is placed in the drawn-out pointed end of the tube and lightly compressed by means of a glass rod. The 5-g. sample of flour is carefully introduced, in small quantities at a time, the tube being held vertically and the flour being allowed to fall into it from a height of 1 to 2 cm. The tube is

then placed in a stand, an extraction flask, of 60ml. capacity, is put underneath the drawn-out end, and ether is poured into the upper part of the tube, so as to fill it completely. The flour is allowed to soak up the ether, and as soon as the first drops fall into the flask the tube is corked. The rate of flow of the liquid is regulated by means of the cork, so as to obtain one drop in approximately 10 seconds. When all the ether has passed through the flour the extraction is complete. The drawn-out part of the tube, which always retains a little of the fat, is washed out with ether into the extraction flask. After evaporation of the solvent the flask is placed in an oven at 100°C . for an hour, and then cooled and weighed.

(NOTE.—The heating is omitted when rancidity is to be determined, and the specified solvent (alcohol, 30; ether, 30; chloroform, 40 per cent.) is substituted for ether.)

This method is simple to use and provided care is taken it is rapid and economical.

L. F. T.

SOLID EXTRACTS

By Ivor Griffith, Ph. M., Sc. D., F. R. S. A.

Despite the form in which this information is presented it may be accepted as trustworthy and up-to-date. Original sources are not listed but they may be obtained upon request.

This nation spends more for its cosmetics and its tobacco than it does for education. It is always surprising how people spend their money. Here is the order of income usage revealed in the highly informative report on consumer expenditures in the U. S. A. just issued by the National Resources Planning Board: Food, 29 per cent.; housing, 16 per cent.; household operation, 9 per cent.; clothing, 9 per cent.; automobile $6\frac{1}{2}$ per cent.; medical care, 4 per cent.; recreation, 3 per cent.; personal care and tobacco, each about 2 per cent.; transportation, $1\frac{1}{2}$ per cent. Education, less than 1 per cent., ranks last except for a few miscellaneous items. Thus about 85 per cent. of the \$59,300,000,000 income in 1935-6 was spent for current consumption, 10 per cent. was saved, 4 per cent. given away to relatives, friends, churches, philanthropies, only $1\frac{1}{2}$ per cent. as income and other personal taxes.

The mels and oxymels were once popular as adjuvant medicinals. Honey long antedated sugar in civilized use, for the busy bee had wings but the sugar cane is static. That is why all primitive peoples used honey in making tasty medicines. But here's a honey of a method of taking medicine. According to reports by Tass, U. S. S. R. news agency, Dr. N. P. Yoirish, Soviet physician and amateur bee-keeper, dissolves various medicines, in sugar syrup and feeds this sweet fare to his bees who compound it invitingly in honeycombs with medicinal strength unimpaired. Sixty brands from the hive-pharmacy containing albumen, bromine, iron, iodine, calcium and other substances, so it is claimed.

An item printed in our last issue concerning the total absence of hay-fever in Japan in spite of the prevalence of indigenous pollen producers brought an expression of doubt from Dr. Durham, mentioned below.

Elsewhere we noted the following item which only adds to an estimate of this botanist's expert knowledge of his subject:

Hay-fever pollens ride the winds over the Atlantic ocean, but only for a relatively short distance off shore, O. C. Durham, chief botanist of the Abbott Laboratories, stated after examining vaselined glass slides exposed by Engineer J. W. Etchison of the Pan-American Airways plane, Yankee Clipper, on a late-summer trip to Europe and return.

Pollens were found at altitudes between 2000 and 8000 feet out to 275 miles off shore, the slides indicated. Above 8000 feet there were practically no pollens over either land or sea. Since the plane did not fly at lower altitudes when far off shore, the possibility still remains that pollens may be present "at the bottom of the air" farther out at sea than the slides showed.

The humble and prolific milkweed is now mentioned as the source of a powerful digestive enzyme.

The quantity of the new-found substance in milkweed juice is small, but it is believed that large-scale and intensive cultivation of the plant might make its production profitable. At present, papaya imports amount to half a million pounds a year, costing several million dollars and largely dedicated to the friendly job of tenderizing erst-while tough chunks and cuts of meat.

The active principle of the milkweed has been named asclepain, from the botanical name of the plant, Asclepias, by analogy with the formation of the word papain from the plant name Papaya.

Another idea for the W. P. A. to keep shovels and pickaxes from rusting through resting too much. Why not start eradicating from the landscape such noxious weeds as the ragweed and poison ivy.

Every vacation season brings evidence that people are becoming more and more poison ivy-minded. The need for a campaign of eradication of this highly dangerous plant is apparent.

At the last legislative session of New Hampshire there was introduced a bill making it the duty of health officers to initiate steps to this end. Evidently, however, the legislature considered that a rather large contract would thus be imposed on our local health officials, and the bill was rejected.

But one of these days it will crop up again, for the New England States are slow to change their holidays but quick to adopt sane practices in public health insurance.

The science of limnology was founded by Forel about 1887, for study of the Swiss lakes, and has had gradual development ever since. At least two or three American colleges offer courses designed primarily to train workers for the more recently developing applied aspects of this still basically pure science. Several states are already fully awakened to the need of taking proper steps to conserve or to increase the fish in their waters. This is especially true of "vacation" states, which offer fishing as an important attraction. New Hampshire has nearly completed a four-year survey that should lead to practical measures both to prevent contamination by industrial wastes, and to aid fishing by building up an ample natural food supply and protective features. More power to New Hampshire.

Textile mills and other users will be interested to learn that they no longer need rely entirely on the vagaries of tropical weather and war-disrupted shipping. For now comes "the synthetic gum."

Though chemically different, this new synthetic gum is reported to have properties similar, and in some cases superior, to those of the natural gums. Its viscosity is said to be high and to be well maintained in both acid and alkaline conditions and even after considerable dilution. It is completely miscible with water. Since it is a synthetic, it can be supplied in uniform quality, an advantage over natural gums, which sometimes pick up strange companions in their travels.

Tiredness, along with "rheumatism, anemia and other common afflictions" may result from lack of vitamin C, it appears from an announcement of research by Dr. Lawrence E. Detrick, research associate in chemistry on the Los Angeles campus of the University of California.

Dr. Detrick believes that the "deep-seated cause" of these conditions is borderline scurvy, due to not eating enough vitamin C. Violent scurvy, due to complete lack of vitamin, is a disease of past history, but borderline scurvy is "more prevalent today than is generally realized," Dr. Detrick stated.

Wounds of animals fed plenty of vitamin C in orange juice healed much faster and withstood greater pressure than those of animals that were given scanty amounts of orange juice, although the latter animals got enough vitamin C to escape severe scurvy.

Please note that Dr. Detrick conducted his research under a grant from the California Fruit Growers Exchange.

BOOK REVIEWS

Done by persons, unafraid to upbraid, but perfectly willing to give praise where praise is really due.

Fundamentals of Pharmacy, Theoretical and Practical. By Blome and Stocking. Cloth-bound, 362 pages, including index, illustrations; published by Lea and Febinger, Washington Square, Philadelphia. Price \$4.50.

This new work on pharmacy is printed because, according to the authors, "there has long been the feeling among teachers of pharmacy that there is a need for a text that treats of this important subject in concise form". While it has been based largely upon "Pharmacy and Dispensing" by Stevens, it is in no sense a revision of any existing text. Incidentally, the book is very kindly dedicated to Dean Stevens.

As might be expected, a work which predicates its existence upon compactness must suffer from lack of completeness. Comparisons are odious, but when we note that the phenomenon of solution is dismissed with five or six pages of printed matter in this work, we also recall that one of the older works in pharmacy fruitfully uses forty pages to discuss the same subject. One could multiply this comparison with almost every chapter heading, thus "Sterile Solutions," etc.

It seems a little surprising that a textbook as new as this should have so very little to say about the more modern phases of the theory and practice of pharmacy. For instance, no mention is made in the text of the newest therapeutic weapons of the sulfanilamide class, nor indeed of any of the dyestuffs used in therapy and in pharmacy. No mention is made of the new ointment bases or of the new surface tension depressants which are finding a large use in modern drug preparations. On the other hand the subject matter within the confines of the book is rather clearly arranged and stated.

The chapter on Hospital Pharmacy is particularly interesting and well illustrated, showing how important a department of the modern hospital the pharmacy department may become with proper handling.

The illustrations are fine throughout, being in most instances picturizations of large-scale manufacturing processes, which seem to be eminently practical in the present aspect of the practice of pharmacy.

The book, according to the reviewer, seems to be compact enough to supply just what the authors imply in their preface, namely, "a working knowledge of the theory and practice of the art that has to

do with the preparation, standardization and preservation of drugs and medicines".

IVOR GRIFFITH.

Industrial Solvents. By Ibert Mellan. 480 pages, 118 tables, 291 charts, graphs and figures. Reinhold Publishing Corp., 330 West 42nd Street, New York, N. Y. 1939. Price \$11.

This is an excellent practical reference book for chemists and others interested in the field of solvents and their industrial uses. Beginning with a presentation of the theories of solvent action, molecular aggregates, viscosity, vapor pressure, boiling point and toxicity the book proceeds to a detailed description and classification, according to chemical composition, of all of the common solvents and many more not so familiar ones. In addition there are 118 tables which provide a great deal of miscellaneous information concerning solvents and 291 charts which illustrate quite clearly the properties of various solvents. Finally the book concludes with a chapter dealing with graphical expression and interpretation as applied to the field of solvents.

L. G. KLECKNER.

Biological Products. By Louis Gershenfeld, P. D., B. Sc., Ph. M. 236 pages, 40 illustrations. Romaine Pierson Publishers, New York, 1939. Price \$4.00.

In the opinion of the reviewer this book is worthy of special attention in that there is available no comparable treatise on the subject. The author has chosen the subject matter and arranged it with relevance, completeness and utility as basic considerations.

Its thirty chapters deal with every type of biological used in the diagnosis and treatment of disease, with those of a related nature being grouped together. The method of preparation, packaging, indications, mode of use, precautions, safeguards, etc., are all considered in detail.

Of unique interest are the numerous bibliographic references which appear *in the text* and not at the end of the book, which this reviewer considers a desirable departure from the usual custom.

The up-to-dateness of the information presented is proven by many inclusions e. g. "Lyovac" packaging, the recently introduced and revolutionary method of supplying certain biologicals in stable form.

This volume can be enthusiastically recommended to physicians, pharmacists and nurses as an excellent handbook in the field of biologicals.

L. F. TICE.